Manufacturing and Production news

Novo Nordisk invests in haemophilia facility

Novo Nordisk is spending 1.5 billion Danish Kroner (£146 million) on a new facility in Kalundborg, Denmark, to produce active pharmaceutical ingredients for haemophilia products.

The new 7,500 m² facility will sit within Novo's huge 1,000,000 m² manufacturing plant in the city. The firm says the move will create 100 new production and engineering jobs in Kalundborg, where Novo Nordisk already employs just under 3,000 people. The new unit will focus on manufacturing haemophilia treatments along with diabetes treatments, which are the company's speciality. The plant, which is expected to be approved and fully operational by 2020, will make active pharmaceutical ingredients for its offering NovoSeven, and will work on future haemophilia products in tandem.

"The investment in Kalundborg underscores our long-term ambition to create and maintain jobs in Denmark.

"This year alone we expect Novo Nordisk will create about 250 new jobs

in Kalundborg, and we are always on the lookout for capable and highly skilled employees," says Henrik Wulff, executive vice president of product supply at Novo Nordisk.

The Danish firm recently also opened a new manufacturing facility in Russia to produce more of its diabetes offerings in the country.

Novartis invests further into generics in Poland

Sandoz, the generics division of Novartis, has opened a large packaging centre in Stryków in Poland.

The move is valued at 171 million Polish Zloty (£30.5 million), making it one of the largest investments in the Polish pharma sector in recent years.

Sandoz already has a large drug manufacturing plant in Stryków that employs 90 people; the five billion tablets it manufactures every year are exported to around 60 countries worldwide.

Sandoz has now added a modern packaging and warehousing centre to the existing manufacturing, production and logistics site in Stryków.

In expanding its existing plant Sandoz has generated an additional 40 posts.

Ard van der Meij who is the president of the board at Sandoz Poland, says: "This investment will greatly facilitate the manufacturing and packaging process, as we will be able to pack around four billion manufactured tablets, without the need to send them to external packaging facilities".

Van der Meij adds: "Poland plays a vital role in our company's growth strategy. This investment will increase the capacity of the plant and, simultaneously, reduce costs. Our decision to expand the Stryków site was motivated by two key considerations: the excellent location of the site, right at the heart of Europe, and the accessibility to highly qualified personnel."

they rarely try to engage CROs in writing development plans and protocols.

This can lead to objectives being agreed which are not deliverable. Clearly, if both parties have bought in to the targets with full understanding, there will be more leverage to get studies back on track when slippage is foreseen. In my experience it's too easy for the contractor to say 'It's not our fault, we didn't know about that'.

Yet there is evidence of major CROs moving away from this level of involvement. Quintiles separated from its investment arm NovaQuest in 2010, which now seems to operate more closely to the Avillion model.

Quintiles may now be putting more effort into advisory services, where it accepts risks associated with its forecasts of outcomes in return for financial benefits.

The sponsor-CRO alliance partner model is a well-worn path now, but Black again detects some erosion here. For example Pfizer and Merck have backed away from it, bringing some functions back in house.

The problem is that even the largest CROs are still much smaller than the largest pharma companies, and still don't offer every possible service. However alliances still arise, for example Biogen, which has selected Quintiles.

But this isn't an exclusive deal, and Biogen is free to use other CROs. A survey in 2014 revealed a possible trend away from single partner alliances; sponsors seem to want the flexibility to select the best partner for a particular job, while building close relationships with a shortlist of contractors.

However this was a common model 20 years ago, when pharma companies set up 'preferred provider' deals. This was very frustrating for younger CROs, who could not break through this 'mega-CRO club' barrier. Many of the lessons learned in contract research can be applied to contract manufacturing. Wellspring Pharma Services identifies a lack of clarity in three main areas: timelines, budgets, and roles.

Sound familiar? They do to me. For the last of these, quality is a major component, especially relating to regulatory compliance.

A breach here could be fatal to a project. It's vital that every quality step has a clearly identified responsible person.

Stepping outside the familiar

CMOs are widely engaged to support clinical trials, and the whole supply chain can be very complex. There are multiple hand-over points between functions.

For example, when a trial overruns, who is responsible for monitoring expiry dates and ordering new stock in good time?

Don't laugh; I have known sponsors to drop the ball here, and not that long ago either. I have even seen a supply chain contract that didn't define one key function at all, and referred to a subsidiary contract that was never actually written.

Perhaps one of the more surprising changes in the CMO arena has been the failure to move inexorably eastwards.

That was predictable as sponsors saw how India and China could offer high volume human resources and lower costs. What they have found is that quality has slipped, partly because of less rigorous inspection regimes in these countries. Hence there seems to have been a retrenchment back to the familiarity of North America and Europe. I might speculate that cultural issues also played a part; collaborating with people of different traditions and cultures is harder work.

Overall, any kind of client-contractor relationship must be underpinned by the competence of both parties.

Freelance consultant Dave Talbot says that the most common cause of project failure is "wishful thinking by the client".

No matter how dictatorial a sponsor may be, in the long run there is far less pain

from challenging their assumptions at the outset, than there will be from committing to unrealistic expectations.

And Kent Hill, a recently-retired freelance consultant, agrees. He cites an unrealistic protocol with selection criteria that mitigates against adequate patient accrual.

The message I get from these comments is that time invested in up-front discussion between the parties is always well spent.

It's a perennial failing in the pharma industry that sponsors are very keen on getting projects started as soon as possible, probably to encourage the shareholders, and spend less time on planning than other high technology industries do. The other benefit of external collaboration is team-building – whatever the project – and should not be underestimated. People get things done, not systems.

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Solutions to blind single and double-blind trials

Industry insight

Today, the labels of investigational products are no longer used as mere carriers of specified contents. They have become multifunctional tools which are able to convey variable data in different languages, blind contents, indicate first opening and product originality or support ease of use.

Research companies in the pharmaceutical industry are frequently faced with the challenge of appropriately blinding the study medication in clinical trials so that the trial investigators, nursing staff, participating patients as well as the persons in charge of handling the data are unaware of the treatment administered to individual patients.

Unwanted biases can only be avoided in this manner. Some blinding solutions can only be used for single-blind trials, some others for double-blind trials.

Avoiding influences

The type of product selected for blinding depends on the primary packaging of the study drugs. Vials, bottles, boxes, tubes and blister packs can be fully covered by a special single and multi-layer label with the necessary dosage instructions. They may be completed with various options like an integrated hoop for hanging a bottle, documentary sections, and security features such as tamper-evident seals or a code-break function that protects trial-specific data against tampering.

Unusual shapes or additional functions tend to require a high level of creativity, know-how and experience from label manufacturers.

Labels are developed individually and tested for criteria such as adhesion and adaptability as well as user-friendliness.

Label performance during application can be simulated at the label supplier or tested at the investigational drug manufacturer's facilities. Often, it is not enough to simply cover up existing labels or surfaces.

The product colour, the glass or even impressions in the glass or plastic can allow conclusions to be drawn as to the contents.

First-class blinding label solutions that are applied at late stage saves both time and costs – by avoiding elaborate colour-matching between liquid placebo and active substance groups in the formulation phase or while searching for a fitting comparator.

Blinding boxes

A blinding box made from opaque cardboard can make the circumference and height of a container, as well as the color of its contents, completely unreconisable. The container is held stable in the centre of the box.

Boxes can be printed on the inside in colour in order to give the active substance and the placebo groups the impression that both trial products are the same colour.

For single-blind trials where the staff involved in the trial are allowed to know how the products are allocated, blinding can take place after the opening is disinfected. For double-blind trials, disinfection can take place after blinding. In both cases, the hypodermic needle can be easily inserted into the container. An integrated control window allows the product to be identified in an emergency. Once opened for the first time, however, it becomes permanently visible. The blinding box can be processed quickly and easily by research companies without the use of tools.

In addition to the blinding box, there is another option featuring an opaque or a transparent plastic cup with a separate lid, into which the container to be masked is placed.

Finally, the cup can be partly or completely covered with a label. Placed directly across the opening area, the label can, at the same time, fulfil a tamper-evident purpose.

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